UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,702	04/15/2002	Camilo Anthony Leo Selwyn Colaco	8830-24	7592

23973 7590 03/22/2007

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/049,702	COLACO, CAMILO ANTHONY LEO SELWYN	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8-11 and 14-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-11, 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8-25-06 has been entered.

The amendment filed 12-22-06 has been entered into the record. Claims 8-11 and 14-16 are pending.

The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

Rejections Maintained

Claims 8-11 and new claims 14-16 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition comprising a complex of heat shock proteins and antigenic peptides from cells infected with an intracellular bacteria, parasite or protozoa, it does not reasonably provide enablement for vaccines for reasons made of record in the Office Actions mailed 5-27-04 and 2-26-06.

Applicants' arguments have been carefully considered but are not persuasive. Applicants cite *In re Marazocchi* and assert that the burden of proof has not been shifted. This is not persuasive, the examiner has provided teaching that provides reasons to doubt the asserted truth of the assertions of the specification that the compositions are useful for vaccines. The teachings of the specification are limited to antibody production and the record indicates that antibody production is generally not know to correlate with protection from infection. Applicants assert that the general teachings cited that provide the state of the art are insufficient to overturn the presumption of adequate teachings

and that the term vaccine is defined as "The term vaccine is used herein to denote to any composition containing an immunogenic determinant which stimulates the immune system such that it can better response to subsequent infections." This is not persuasive because the immune system does not respond "better" to subsequent infection and that the term vaccine as used herein is repugnant to the art. Applicants' own characterization of the examples of the specification at page 5 of the response indicate that "the memory response are shown to be particularly effective as the antibody titer is shown to be at a level of 1:1-10,000, which is the same order of magnitude as the antibody titer seen following the initial inoculation as taught in Example 3, which also refers to antibody titers of 1:1-10,000. Therefore, even by Applicants definition the immune system does not respond "better" because it responds to the same level as the initial inoculation. This is Applicants own characterization of the teachings of the specification. Therefore, given Applicants own characterization of his work and repugnant definition of vaccine in the specification, the claims are not enabled for vaccine. The immune system does not respond "better". Further, given the conventional and well-established definition the teachings in general are sufficient to doubt the asserted truthof the teachings of the specification for all the reasons made of record.

Applicants argue that the generalization that antibody response does not correlate with protection from infection is rebutted by the fact that complexes of antigens with stress proteins do indeed provide for protective responses and relies upon complexes of the stress protein GP96 with tumor antigens that result in reduced tumor growth as compared to unvaccinated controls. The fact that the tumor grew in vaccinated individuals does not provide for protection, it provides for a therapeutic response. Applicants rely again on Colaco et al that indicate a stress protein/peptide complex against tuberculosis was protective. This is not persuasive because the stress/protein peptide complexes were not produced by the claimed method and there is no evidence of record that the method produces the complexes of the prior art. Further, the specification must have

been enabling at the time the invention was made and developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing (*In re Wright*, 27 USPQ2d 1510). The specification neither discloses nor contemplates the HspC prep of Colaco et al. Colaco et al teach that the HspC but not the Hsp65 chaperoned by the mycobacterial vaccine candicates. Therefore, Colaco et al teach that not all heat shock proteins provide for stimulation of an immune response.

Applicants assert that the long-term memory response is indicative of a protective immune response. This is not persuasive because long term antibody memory response can only be protective if the presence of antibody correlates with protection from infection. In the instant case, no evidence is presented that the antibody response is indicative of protection from infection from intracellular parasites/microorganisms. Antibody responses without more information cannot predict the likelihood of protection from infection. Such was well established in the art. Applicant's comments with respect to claim 14 are not understood as claim 14 is not so limited. Further, claim 16 which appears to be representative is not limited according to the recited scope of enablement as set forth in the office actions of record.

The rejection of record is maintained.

Claims 8-11 and 14-16 stand rejected under 35 USC 102(e) as being anticipated by Srivastava et al (US Patent 6,048,530) or in the alternative as obvious under 35 U.S.C. 103(a) as being unpatentable over Srivastava et al (US Patent 6,048,530) for reasons made of record in the office action mailed 5-27-04.

Applicant's arguments have been carefully considered but are not persuasive. Applicants argue the induced nature of the stress proteins of the invention. This is not persuasive, because Srivastava et alt each that "The major stress proteins can accumulate to very high levels in stressed cells, but they occur at a low to moderate levels in cells that have not been stressed." (column 11. lines 24-35). Therefore, the stress-protein

complexes are present in non-stressed cells also and can be "induced". The "induction" does not provide for any necessary differences. The "extraction step" does not provide a unique collection or unique stress-protein complexes that are not present in the non-induced heat-treated infected cells. Applicants argue that the step of "inducing" provides for a more immunogenic stress-protein antigenic fragment complexes than that constitutively expressed by the cell. This is not persuasive, the comparison is for TNF-stress induced proteins produced by the method of Example 1 and not a mere extract as claimed. Further, the amount of protein administered is not set forth in the claims and the induction of increased stress-proteins by heat according to Srivatasva et al would account for higher levels of immunogenicity by virtue of more complex present in the immunization. The comparison in Example 4 is not a finding that there are different complexes present or different immune responses present. To reiterate, the difference in level of immunity is not a showing that the compositions are different, but could be easily accounted for by administering more complexed protein. The dose effect of proteins on the level of antibody or immune response is well established in the art (Abbas et al, in Cellular and Molecular Immunology WB Saunders Company, Philadelphia, PA, 1991, page 219, column 2, see point 2). The effect of stressors such as heat on inducing more protein is also well established and taught by this art. There is no evidence that the complexes per se are different. Applicants argue that it is suprizing that the induced complexes are "more immunogenic" than the non-induced complexes. This is not persuasive, the induction of more complexes by treating with stress provides for a higher level of stress proteins in the lysate and therefore logically a higher immune response because there is more immunogen present in the immunogenic composition. The results are in no way unexpected. More complexes present indicate higher immune response. There is no indication that the response was directed to the intracellular microorganism or mammalian cell components as the immunization lystate was used to determine antibody level and not the microorganism per se.

The rejection as anticipated or obvious is maintained.

Citation of Relevant Art

Bermudez et al (Immunology and Cell Biology, 75:35-40, 1997) teach that expression of protein in *M. avium* varies according to the mammalian cell bacteria are exposed to and is influenced by the stage of intracellular infection (see page 35, abstract).

New Rejections Based on Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 10, 11, 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to independent claim 8 and dependent claims 10, 11, 14 and 15, the claims recites "...stress protein complexed to and an antigenic...". Appears to be missing textual information. Correction is required.

As to independent claim 8 and dependent claims 10, 11, 14 and 15, the claims are confusing because it is unclear as to what has been subjected to stress, the intracellular pathogen or the cell infected with the intracellular pathogen. Clarification is respectfully requested.

Status of Claims

Claims 8-11 and 14-16 stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can generally be reached on M-Th 6:30 am - 6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Jeffrey Siew can be reached on 571-272-0787.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patricia A. Duffy

Primary Examiner

Art Unit 1645